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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/869,741	01/09/2002	Leonard Sciorra	13257.00044	8516

34055 7590 10/05/2005

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EXAMINER	
DO, PENSEE T	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 10/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/869,741	SCIORRA ET AL.	
	Examiner	Art Unit	
	Pensee T. Do	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-92* is/are pending in the application.

4a) Of the above claim(s) *40-92* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-92* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10-10-01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group I, claims 1-39, in the reply filed on May 9, 2005 is acknowledged. The traversal is on the ground(s) that there is a same special technical feature for the two group, such feature is that the magnetic field of the apparatus of group II must be variable in order to achieve the pre-determined increase to carry out in the method of group I. This is not found persuasive because pre-determined increase in the magnetic field strength can be set or carried out using a set of magnets having increasing magnetic fields lining up spatially in the same plane and the particles can flow through horizontally along the plane of the substrate.

The requirement is still deemed proper and is therefore made FINAL.

Claim Objections

Claim 1 is objected to because of the following informalities: Claim 1, line 5 recites "anon" which seems to be a mistype. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 29 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 29 is indefinite for reciting a "coating step" which lacks antecedent support.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-9, 12, 14, 16-20, 22-24, 29, 37-39 are rejected under 35 U.S.C. 102(b) as being anticipated by Farber (US 5,602,042).

Farber teaches a method and apparatus for magnetically separating biological particles from a mixture. The method comprises providing superparamagnetic beads coated with a ligand with specific affinity to target molecules; combining the sample suspected of containing the target molecules with such beads to form a mixture; exposing the mixture to a plate with a collection surface so that the beads flow through the fluid toward the magnetic field source so that the target molecules are collected against the plate surface. The target molecules can be transferred out of the plate from the fluid by a transfer element. The sample comprises of various cells, proteins, viruses, and other particles, both biological and non-biological. The target molecules can be a population of cells or a subpopulation of a cell type and it is inherent that the undesired components of the sample are the other subpopulations other cells. (see col. 3, lines 1-44). The magnet and the plate are configured to direct the flow of tagged particles to selected portions of the plate surface. For examples, the magnet element can be arranged with the plate element so that the generated magnetic field is stronger at selected areas of the plate surface. The provision of a spatially varying magnetic field

enables the device to control the spatial distribution of the cells collected against the plate. The magnet element is positioned vertically above the plate, and couples to the plate at selected locations for providing a stronger magnetic attraction at these locations. Since the magnetic attraction at certain locations are stronger than those at the other locations, the magnetic field must be increased at predetermined strength. (increasing at predetermined magnetic field strength)(col. 3, line 65-col. 4, line 10). Alternatively, the magnet element can be fixed at one point on the periphery of a rotating disc that is disposed vertically above the plate. The rotating disk moves the magnet element relative to the plate to spatially vary the magnetic field. Other configurations for spatially varying the magnetic field can use a distributed array of magnet elements that can be selectively activated and deactivated. (pulsing) (see col. 3, line 59-col. 4, line 11). The device in Figure 1, illustrates a series of posts 30 that allows the strength of the magnetic field to be varied over the area of the surface 42. The magnet control system 14 (fig. 1) selectively activates the posts 30 and thus generates a spatially-varying and time-varying magnetic field. It is inherent that the activating and deactivating of the magnetic field is performed at a frequency such that the pulses overlap in time since Farber teaches the control system activates and deactivates posts that generates a time-varying magnetic field. The resultant varying magnetic field causes the magnetically-induced movement of the particles and the particles 28 are distributed across the surface of the plate 16 by the selectively activated posts. (see col. 11, lines 20-37; col. 7, lines 35-50). The magnetic particles adhering to the plate can be removed from the plate by deactivating the magnetic field and are

collected against a receiver by a transfer system. (see col. 11, lines 44-50). The method also comprises a step of removing the magnetic particles from the target substance (see col. 5, lines 1-9). Although Farber does not explicitly teach that the magnetic particles have uniform physical and magnetic properties, these properties are inherent because Farber teaches that the magnetic particles are superparamagnetic particles, and have a diameter greater than 1 micron. (see col. 4, lines 55-58). The present invention also teaches that the magnetic particles are superparamagnetic and have diameter around 0.05 to 4.5 microns. Thus, since the type and the size of magnetic particles in Farber are the same as those of the present invention, it is inherent that Farber's magnetic particles have uniform physical and magnetic properties and are substantially identical. Farber teaches that that fluid sample can be a liquid sample of a biological material such as sera, that contains a variety of components including cells, proteins or other biological material. The target or desired components can be a specific subpopulation of cells. The moieties on the surface of the particles are antibodies. (see col. 9, lines 30-48). A sample of sera contains at least cells and proteins. Thus, when cells are the targets and separated from the sera sample, the proteins must be the undesired portions of the sample. Regarding claim 24, it is inherent that the non-target component migrates at a different rate than that by target which are conjugated to magnetic particles because magnetic particles migrates can migrate at a faster rate due to the magnetic fields being imposed. The magnetic mixture is placed along one edge of the substrate material. (see fig. 1). The magnetic field has a strength that varies substantially linearly with distance within the plane of the substrate. (see col. 3, line 59-

col. 4, line 11). For claim 14, Farber teaches that the microbeads can be magnetically responsive particle having an exterior surface coated with a layer of material suitable for absorbing one or more biological protein molecules. (see col. 9, lines 49-52). Regarding claim 23, since Farber teaches target substance is separated from the sample, it is inherent that such target substance is the undesired component of the sample because the concentration of the undesired components in the sample is inversely associated with the concentration of the desired components in the sample. Thus, when the bound and unbound portions of a sample are separated, either portion can be the desired components to be studied and that would leave the other portion undesired.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 32-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Farber (US 5,602,042).

Farber has been discussed above.

However, Farber fails to teach the frequency at which the magnetic field is activated or deactivated is from about 0.5 to 10 seconds per pulse or 2.0 second per pulse; a magnetic field strength to be about 1.5 to 2.0 or at least 3.0 Tesla

Since Farber teaches that his magnetic field can be activated or deactivated to flow the magnetic particles across the substrate, it would have been obvious to one

having ordinary skills in the art at the time the invention was made to arrive at these specific pulse ranges or magnetic field strength since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233.

Claims 10, 11, 13, 15 , 21 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Farber (US 5,602,042) in view of Terstappen et al. (US 5,646,001).

Farber has been discussed above.

However, Farber fails to teach that the magnetic particles include at least two different magnetic particles with different physical or electromagnetic properties; wherein the moieties on the surface of the magnetic particles are capture agents that bind to at least one ligand that binds to the target substance; the capture agents bind to more than one ligand; wherein the sample is from maternal blood and the desired component is fetal cell and the undesired component is maternal cell. Farber also fails to teach labeling the target substance with a fluorescent marker.

Terstappen teaches a method for separating and releasing one or more selected subset of biological entities from a mixed population. The method comprises providing a plurality of capture agents comprising a receptor which specifically binds, either directly or indirectly, to a solid support to the character determinant of the first subset and at least a second capture agent comprising a receptor which specifically binds, directly or indirectly, to the characteristic determinant of one other subset. The sample is added to the those capture agents. Magnetic field is applied to separate those subsets from the rest of the sample. (see col. 4, line 55-col. 5, line 15). One type of receptor binds to the

a highly magnetic bead and another type is bound to a bead with a low magnetic saturation (different beads with different electromagnetic property). Separation in a high gradient magnetic field would capture both types of beads. Removal from the field to a weaker magnetic separation would result in a specific retention of biological substances bound to highly magnetic beads. (see col. 12, lines 54-65). Terstappen also teaches that the specific cell types are fetal cells present in the maternal blood (see example 16, col. 5, line 34). The specific binding substance used are anti-haptens, anti-lectins, peptides, protein A & G, etc. (see col. 7, lines 55). These are the same substances those claimed in the present invention. (see the present specification, page 26, lines 13-20). The method also comprises a step of selective releasing the target cells from the magnetic particles and isolating the released target cells. For detection, the target cells can be linked to a fluorescent label (see col. 19, lines 1-20).

It would have been obvious to one of ordinary skills in the art to use different magnetic particles with different electromagnetic property as taught by Terstappen in the method of the Farber to separate more than one subset of target substances in a mixed population simultaneously and thus much time and effort can be saved. One skilled in the art would have a reasonable expectation of success when modifying the method of Farber using more than one magnetic particles with different property because they both teaches varying magnetic field strengths when separating a mixed population of cells and releasing cells from the magnetic particles. It would have been obvious to one of ordinary skills in the art to add a fluorescent label to the released target cells as taught by Terstappen in the method of Farber because Farber also

teaches releasing target cells/biological substances after separation for detection. Regarding claim 13, since Terstappen teaches that the ligands for specific binding are the same as those ligands in the present invention and the ligand can bind to the solid phase directly or indirectly, it would have been obvious to one of ordinary skills in the art to use the indirect method of binding specific substances as taught by Terstappen to the magnetic particles of Farber for an indirect affinity binding. Such indirect binding is known for providing high affinity and specificity between the solid phase and the ligand so that the target can be stably captured. Regarding claim 15, since the specific binding substance taught by Terstappen are the same as capture agents of the present invention, it is inherent that the specific binding substance of Terstappen can bind to the more than one ligand which binds to the target substance in an indirect binding approach. Regarding claim 21, it would have been obvious to one of ordinary skills in the art to separate fetal cells and maternal cells since both reference teaches separating cells and maternal cells and fetal cells are often genetically studied.

Claims 25-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Farber (US 5,602,042) in view of Mroczkowski et al. (US 5,137,827).

Farber has been discussed above.

However, Farber fails to teach that the substrate material is methylcellulose and that the substrate material comprises a viscous solution that prevents diffusion of the magnetic component unless a magnetic force is applied; the solution is between 1.7% and 2% methycellulose.

Mroczkowski teaches that methylcellulose is a bioreactive plastic. (see col. 9, lines 50-55).

Since it is well known in the art that methylcellulose is a plastic, it would have been obvious to one of ordinary skills in the art to make a plate/substrate using plastic such as methylcellulose as taught by Mroczkowski for use in the method of Farber since Farber teaches that his plate is made of a conventional plastic. (see Farber col. 5, lines 54-56). Methylcellulose is also known as for a growth culture media and a viscous solution. Thus, it would have been obvious to one of ordinary skills in the art to recognize the properties of methylcellulose since the substrate material is the same as that of the present invention and that the separation involves populations of cells and thus culture media is needed for maintaining the physiological environment and vitality of those cells. Regarding claim 27, it would have been obvious to one having ordinary skills in the art at the time the invention was made to use methycellulose at a range of 1.7% to 2 % since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233.

Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over Farber (US 5,602,042) in view of Tseng-Law et al. (US 6,017,719).

Farber has been discussed above.

However, Farber fails to teach labeling non-target substance with a fluorescent marker.

Tseng-Law teaches a positive or negative methods of cell selection from a heterogeneous cell suspension containing undesired cells having a second antigen. The positive selected cells are labeled with a fluorescent marker. (see abstract; col. 4, lines 40-63; col. 21, line 65-col. 22, line 10).

It would have been obvious to one of ordinary skills in the art to incorporate a step of positive selection and label the non-target selected cells with a fluorescent marker as taught by Tseng-Law in the method of Farber since both references teaches using magnetic particles to separate a heterogeneous mixture of cells so that undesired cells can be confirmed that they are eliminated from the mixture.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 571-272-0819. The examiner can normally be reached on Monday-Friday, 7:00-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Pensee T. Do
Patent Examiner
September 25, 2005

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10/03/05